16/627,368

Crane 10/766403

05/18/2006

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FILE 'CAPLUS' ENTERED AT 10:42:53 ON 18 MAY 2006

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FILE COVERS 1907 - 18 May 2006 VOL 144 ISS 21 FILE LAST UPDATED: 16 May 2006 (20060516/ED)

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'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> file registry FILE 'REGISTRY' ENTERED AT 10:43:04 ON 18 MAY 2006 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 16 MAY 2006 HIGHEST RN 884586-69-0 DICTIONARY FILE UPDATES: 16 MAY 2006 HIGHEST RN 884586-69-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

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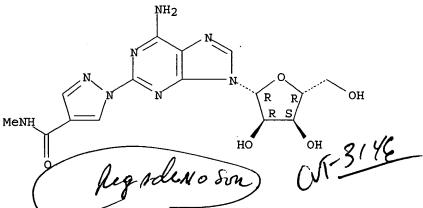
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information

NAME)

Absolute stereochemistry.



L20 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:131938 CAPLUS

DOCUMENT NUMBER:

144:247600

TITLE:

Tachycardia caused by A2A adenosine receptor agonists is mediated by direct sympathoexcitation in awake rats Dhalla, Arvinder K.; Wong, Mei-Yee; Wang, Wei-Qun;

AUTHOR(S): Dhalla

Biaggioni, Italo; Belardinelli, Luiz

CORPORATE SOURCE:

Department of Pharmacology, CV Therapeutics, Palo

Alto, CA, USA

SOURCE:

Journal of Pharmacology and Experimental Therapeutics

(2006), 316(2), 695-702 CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER:

American Society for Pharmacology and Experimental

Therapeutics

DOCUMENT TYPE:

Journal

LANGUAGE:

English

Adenosine-induced tachycardia is suggested to be mediated via A2A receptors; however, the exact mechanism for this effect remains to be understood. The present study was carried out using regadenoson, a selective A2A adenosine receptor agonist, to determine the role of the A2A receptor subtype in adenosine-induced tachycardia. Regadenoson (0.3-50 μg/kg) given as a rapid i.v. bolus to awake rats caused a dose-dependent increase in heart rate (HR). Mean arterial pressure (MAP) increased at lower doses, whereas at higher doses, there was a decrease in MAP. The increase in HR was evident at the lowest dose (0.3 μg/kg) of regadenoson at which there was no appreciable decrease in MAP. Pretreatment with 30 µg/kg ZM 241385, an A2A receptor antagonist, attenuated the decrease in MAP and the increase in HR caused by regadenoson. Pretreatment with metoprolol (1 mg/kg), a β -blocker, attenuated the increase in HR but had no effect on the hypotension caused by regadenoson. In the presence of hexamethonium (10 mg/kg), a ganglionic blocker, the tachycardia was completely prevented even though MAP was further reduced. Regadenoson treatment (10 µg/kg) significantly increased plasma norepinephrine levels almost 2-fold above baseline. The dissociation of HR and MAP effects by dose, time, and pharmacol. interventions provides evidence that tachycardia caused by regadenoson is independent of the decrease in MAP and may not entirely be baroreflex-mediated, suggesting that regadenoson may cause a direct stimulation of the sympathetic nervous system via activation of A2A adenosine receptors.

IT 313348-27-5, Regadenoson

RL: PAC (Pharmacological activity); BIOL (Biological study)

presence of reversible hypoperfusion was 86%. The 400-μq dose was better tolerated. Overall, regadenoson was well-tolerated; side effects (e.g., chest discomfort, flushing, dyspnea) were generally mild in severity and self-limiting. High-grade atrioventricular block and bronchospasm were not observed Conclusions: Regadenoson is well-tolerated and seems as effective as adenosine for detecting and quantifying the extent of hypoperfusion observed with SPECT perfusion imaging. Phase III clin. trials are now underway, given the promise of regadenoson's reduced side effects and simplicity of bolus administration.

313348-27-5, Regadenoson

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); BIOL (Biological study)

(A2A adenosine receptor agonist regadenoson with $400-\mu g$ dose combined with SPECT myocardial perfusion imaging was well-tolerated, effective with mild side effects for detecting reversible myocardial hypoperfusion in ischemia patient)

RN 313348-27-5 CAPLUS

CN Adenosine, 2-[4-[(methylamino)carbonyl]-1H-pyrazol-1-yl]- (9CI) NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS 18 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Property of the second

L20 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2005:146593 CAPLUS

DOCUMENT NUMBER:

142:347942

TITLE:

Regadenoson: Adenosine A2A agonist adjunct for

myocardial perfusion imaging

AUTHOR(S):

Sorbera, L. A.; Castaner, J.; Leeson, P. A

CORPORATE SOURCE:

Prous Science, Barcelona, 08080, Spain

SOURCE:

Drugs of the Future (2004), 29(10), 998-1002 CODEN: DRFUD4; ISSN: 037-8282

PUBLISHER:

Prous Science

DOCUMENT TYPE:

Journal; General Review

LANGUAGE:

English

A review. Coronary vasodilators such as adenosine and dipyridamole, commonly used in pharmacol. stress testing, stimulate adenosine A2A receptors. However, both agents also nonselectively stimulate A1, A2B and A3 receptor subtypes, resulting in a high incidence of adverse events. Research efforts continue in an attempt to develop novel pharmacol. stress agents with fewer unwanted side effects, more selective A2A receptor-agonist effects and which can be administered as a bolus instead; of by infusion to produce selective vasodilatation with a rapid onset and short duration of action. Regadenoson is a novel low-affinity A2A

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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
             TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                            US 2002-399176P
                                                                P 20020729
                                            US 2002-399177P
                                                                   20020729
                                            US 2002-426902P
                                                                   20021115
                                            US 2003-459803R
                                                                   20030402
                                            US 2003/629386
                                                                A2 20030729
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AB A myocardial imaging method that is accomplished by administering one or more adenosine A2a adenosine receptor agonist to a human undergoing myocardial imaging as well as pharmaceutical compns. comprising at least one A2a receptor agonist, at least one liquid carrier, and at least one co-solvent. CVT-3146 is a useful pharmacol. stress agent for myocardial perfusion imaging. CVT-3146 is formulated in a liquid carrier comprising sodium chloride, sodium bicarbonate, EDTA, methylboronic acid and propylene glycol. It is administered as an i.v. bolus.

IT 313350-86-6, CVT 3033

RL: DGN (Diagnostic use); PAC (Pharmacological activity); BIOL (Biological study); USES (Uses)

(formulation of adenosine receptor agonists as pharmacol. stress agent for myocardial perfusion imaging)

RN 313350-86-6 CAPLUS

CN Adenosine, 2-(1-pentyl-1H-pyrazol-4-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 313348-27-5, CVT 3146

RL: DGN (Diagnostic use); PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); BIOL (Biological study); PROC (Process); USES (Uses)

(formulation of adenosine receptor agonists as pharmacol. stress agent for myocardial perfusion imaging)

RN 313348-27-5 CAPLUS

CN Adenosine, 2-[4-[(methylamino)carbonyl]-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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1 687 1 to 1

REFERENCE COUNT:

15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN ACCESSION NUMBER: 2004:101001 - CAPLUS

DOCUMENT NUMBER:

140:141803

TITLE:

Myocardial perfusion imaging using A2A receptor

agonists

INVENTOR (S):

Belardinelli, Luiz

PATENT ASSIGNEE (S):

CV Therapeutics, Inc., USA

SOURCE:

PCT Int. Appl., 66 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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EP 1524984				A1			0427											
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JP	2005	5381	90		T2	:	2005	1215	1	JP 2	005-		20030729					
WO	2005	0823	79		Al		2005	0909	1	WO 2	004-		20040127					
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		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
		ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	ŪĠ,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW	

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REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN ACCESSION NUMBER: 2003:875101 CAPLUS DOCUMENT NUMBER: 139:358763 TITLE: (Inhibition of platelet aggregation with glycoprotein Porter, Stephen R.; Fitzgerald, Desmond Joseph VDDI Pharmaceuticals, USA PCT Int. Appl., 28 pp.
CODEN: PIXXD2
Patent
English
1 IIb/IIIa receptor antagonist INVENTOR(S): PATENT ASSIGNEE(S): SOURCE: DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. APPLICATION NO. KIND DATE DATE WO 2003-US12515 WO 2003090733 **A1** 20031106 20030423 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, **67**77多年,59年, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 2003223702 20031110 AU 2003-223702 A1 20030423 PRIORITY APPLN. INFO.: US 2002-374860P 20020423 WO 2003-US12515 W 20030423 AB The present invention provides methods and compns. for preventing platelet aggregation and for treating individuals suffering from conditions or undergoing procedures that may result in unwanted platelet aggregation. In particular the invention provides methods and compns. for arterial vessel pacification. The methods are based on the administration of a

therapeutically effective amount of a glycoprotein IIb/IIIa receptor antagonist, e.g., xemilofiban. The treatment may commence prior to a medical or surgical procedure or an outbreak of a condition, either of which results in the activation of platelets that may lead to thrombus formation, and may continue thereafter.

IT 313348-27-5, CVT 3146

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);

US 2003-652378

A1 20030829

OTHER SOURCE(S):

MARPAT 139:323754

AB 2-Adenosine N-pyrazole compds. I wherein R1 is CH2OH, amide, R2 and R4 are H, alkyl, aryl, R3 is alkyl, halo, NO2, CN, ether, thio ether, amine, sulfone, sulfonamide, ester, and methods for using the compds. as A2A receptor agonists to stimulate mammalian coronary vasodilatation for therapeutic purposes and for purposes of imaging the heart. Thus, I (R1 = OH, R2 = R4 = H, R3 = CO2Et) was prepared its affinity for the adenosine A2a receptor (Ki = 10-1000 nM), is reported. All compds. show moderate selectivity for human A2A vs. A1 receptor.

IT 313348-27-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nucleoside N-pyrazole as adenosine A2a receptor agonists for purposes of imaging the heart)

RN 313348-27-5 CAPLUS

CN Adenosine, 2-[4-[(methylamino)carbonyl]-1H-pyrazol-1-yl]- (9CI) (CA INDEX

Absolute stereochemistry.

REFERENCE COUNT:

18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS

REFERENCE COUNT:

31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:92399 CAPLUS

DOCUMENT NUMBER:

138:131113

TITLE:

Method and compositions using A2A adenosine receptor agonists and type IV phosphodiesterase inhibitors for

treating the inflammatory response

INVENTOR(S):

Linden, Joel M.; Sullivan, Gail W.; Scheld, W. Michael

University of Virginia Patent Foundation, USA;

University of Virginia

SOURCE:

U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 320.769,

abandoned.
CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT ASSIGNEE(S):

700 0311313	PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
PRIORITY APPLN. INFO.: US 1994-272821 US 1994-272821 US 1994-272821 A2 1994073 US 1998-3930 B2 1998010	-/					
PRIORITY APPLN. INFO.: US 1994-272821 A2 1994073 US 1998-3930 B2 1998010	AUS 6514949	B1	20030204	US 2000-634407		20000809
US 1998-3930 B2 1998010	US 5877180	Α	19990302	US 1994-272821		19940711
	PRIORITY APPLN. INFO.:			US 1994-272821	A2	19940711
US 1999-320769 B2 199905				US 1998-3930	B2	19980108
	PACE TO CONTRACT OF A SECRET 1.			US 1999-320769	B2	19990527

OTHER SOURCE(S):

MARPAT 138:131113

AB Agonists of A2A adenosine receptors, optionally in combination with a Type IV phosphodiesterase (PDE) inhibitor, are effective for the treatment of the inflammatory response of mammalian tissue.

IT 313348-27-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(A2A adenosine receptor agonist and type IV phosphodiesterase inhibitor for treating inflammatory response)

RN 313348-27-5 CAPLUS

CN Adenosine, 2-[4-[(methylamino)carbonyl]-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

vasodilation during myocardial perfusion imaging for noninvasive detection of subcrit. arterial stenosis.

IT 313348-27-5, CVT 3146

RL: DGN (Diagnostic use); PAC (Pharmacological activity); BIOL (Biological study); USES (Uses)

(selective A2A adenosine receptor agonist CVT-3146 as a coronary vasodilator in conscious dogs: potential for use in myocardial perfusion imaging)

RN 313348-27-5 CAPLUS

CN Adenosine, 2-[4-[(methylamino)carbonyl]-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2002:732391 CAPLUS

DOCUMENT NUMBER:

138:362124

TITLE:

Structure-affinity relationships of the affinity of 2-pyrazolyl adenosine analogues for the adenosine A2A

receptor

AUTHOR (S):

Palle, Venkata P.; Elzein, Elfatih O.; Gothe, Scott

A., Li, Zhihe; Gao, Zhenhai; Meyer, Stephanie;

Plackburn, Brent; Zablocki, Jeff A.

CORPORATE SOURCE:

CV Therapeutics, Department of Bioorganic Chemistry,

Palo Alto, CA, 94304, USA

SOURCE:

PUBLISHER:

Bioorganic & Medicinal Chemistry Letters (2002)

12(20), 2935-2939

CODEN: BMCLE8; ISSN: 0960-894X

Elsevier Science Ltd. : Journal

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S):

CASREACT 138:362124

The structure-affinity relationships of two novel 2-substituted adenosine series containing a substituted pyrazole attached at the N-1 or C-4 position for the adenosine (ADO) A2A receptor are described. Compds. in the 2-(N-1-pyrazolyl) adenosine series provided the highest affinity for the ADO A2A receptor as compared to the 2-(C-4-pyrazolyl) series. The main structural differences between the two series point to the N-1 nitrogen imparting favorable binding interactions with the receptor.

IT 313348-27-5P 313350-86-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

CVT-3146, 2-(N-1-(4-N-methylcarboxamidopyrazolyl)) adenosine derivative and compound CVT-3033, 2-(4-(1-N-pentylpyrazolyl)) adenosine derivative, were found to be short acting functionally selective coronary vasodilators (CV t0.5 = 5.2±0.2 and 3.4±0.5 min, resp. - rat isolated heart 50% reversal time) with good potency (EC50S = 6.4±1.2 nM and 67.9±16.7 nM, resp.), but they possess low affinity for the ADO A2A receptor (Ki = 1122±323 nM and 2138±952 nM, resp.; pig striatum).

IT 313348-27-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(2-substituted PI system derivs. of adenosine as coronary vasodilators acting via A2A adenosine receptor)

RN 313348-27-5 CAPLUS

CN Adenosine, 2-[4-[(methylamino)carbonyl]-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 313350-86-6

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(2-substituted PI system derivs. of adenosine as coronary vasodilators acting via A2A adenosine receptor)

RN 313350-86-6 CAPLUS

CN Adenosine, 2-(1-pentyl-1H-pyrazol-4-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$NH_2$$
 NH_2
 NH_2

REFERENCE COUNT:

22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

والجادة فالمتابات

RN 313350-86-6 CAPLUS

CN Adenosine, 2-(1-pentyl-1H-pyrazol-4-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L20 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:454277 CAPLUS

DOCUMENT NUMBER: 135:266911

TITLE: Novel short-acting A2A adenosine receptor agonists for

coronary vasodilation: inverse relationship between affinity and duration of action of A2A agonists

AUTHOR(S): Gao, Zhenhai; Li, Zhihe; Baker, Stephen P.; Lasley,

Robert D.; Meyer, Stephanie; Elzein, Elfatih; Palle,

Venkata; Zablocki, Jeff A.; Blackburn, Brent;

Belardinelli, Luiz

CORPORATE SOURCE: Departments of Pharmacological Sciences, CV

Therapeutics, Palo Alto, CA, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics

(2001), 298(1), 209-218

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental

Therapeutics

DOCUMENT TYPE: Journal LANGUAGE: English

AB Several potent and selective A2A adenosine receptor agonists are currently available. These compds. have a high affinity for the A2A receptor and a long duration of action. However, in situations where a short duration of action is desired, currently available A2A receptor agonists are less than ideal. From a series of recently synthesized A2A receptor agonists, two agonists (CVT-3146 and CVT-3033) with low affinity were selected for further characterization as selective and short-acting coronary

REFERENCE COUNT: THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN 2000:911270 CAPLUS

27

ACCESSION NUMBER:

DOCUMENT NUMBER:

134:56921

TITLE:

Preparation of nucleoside N-pyrazole as adenosine A2a receptor agonists for purposes of imaging the heart

INVENTOR(S):

Zablocki, Jeff A.; Elzein, Elfatih O.; Palle, Venkata

PATENT ASSIGNEE(S):

CV Therapeutics, Inc., USA PCT Int. Appl., 56 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

	PAT	PATENT NO.						KIND DATE			APPLICATION NO.						DATE			
		2000078779 2000078779						2000		Ī	WO 2	000-		20000621						
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INVENTOR(S):

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CV Therapeutics, Inc., USA PCT Int. Appl., 55 pp.

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